REMARKS

Claims 1-4 are pending in the instant application. With this Amendment, Claim 2 is canceled without prejudice, Claims 5 and 6 are added and Claims 1, 3 and 4 are amended. Thus, after entry of the present Amendment, Claims 1 and 3-6 are pending in the present application. For the PTO's convenience, a clean copy of pending Claims 1 and 3-6 are attached hereto as Exhibit B.

I. THE AMENDMENT TO THE CLAIMS

Applicants have canceled Claim 2 without prejudice, and Applicants have amended Claims 1, 3 and 4 to correct minor errors in claim language and to conform with the election of SEQ ID NOS:9-18 for prosecution on their merits.

Applicants have added new Claims 5 and 6. New Claims 5 and 6 are fully supported by the specification and claims as originally filed. For instance, new Claim 5 is supported in the specification, for example, at page 16, lines 1-6, and by original Claim 1. New Claim 6 is supported in the specification, for example, at page 16, lines 22-30, and at page 13, lines 2-28.

As the amendments are fully supported by the specification and claims as originally filed, thet does not constitute new matter. Entry thereof is respectfully requested.

II. SEQ ID ELECTION

Applicants hereby elect SEQ ID NOS:9-18 for prosecution on their merits. Applicants have amended Claims 1, 3 and 4 to conform with this election.

III. THE REJECTION UNDER 35 U.S.C. § 112, FIRST PARAGRAPH (DEFINITENESS)

Claims 1, 3 and 4 stand rejected under 35 U.S.C. § 112 as allegedly being indefinite. The PTO asserts that Claims 1-4 are drawn to non-elected SEQ ID NOS. Applicants have amended Claims 1, 3 and 4 to recite the elected SEQ ID NOS.

The PTO also asserts that the phrase "first disclosed" is indefinite. Although the meaning of the phrase "first disclosed" is readily apparent to one of skill in the art, in order to expedite prosecution, Applicants have deleted the phrase "first disclosed" from amended Claims 1 and 3.

Applicants submit that the rejections under 35 U.S.C. § 112 for alleged indefiniteness are moot and request that they be withdrawn.

IV. THE REJECTION UNDER 35 U.S.C. § 101

Claims 1, 3 and 4 stand rejected under 35 U.S.C. § 101 as allegedly lacking patentable utility. Applicants respectfully traverse the rejection on the ground that Claims 1, 3 and 4 are patentably useful.

According to 35 U.S.C. § 101, whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter may obtain a patent therefor subject to the conditions and requirements of 35 U.S.C. The threshold of utility is not high. *Juicy Whip Inc. v. Orange Bang Inc.*, 51 USPQ2d 1700, 1702 (Fed. Cir. 1999). An invention is "useful" under 35 U.S.C. § 101 if it is capable of providing some identifiable benefit. *Id.* (*citing Brenner v. Manson*, 383 U.S. 519, 534, 148 USPQ 689, 695 (1966)).

Claims 1 and 3-6 recite synthetic oligonucleotides or isolated polynucleotides corresponding to SEQ ID NOS:9-18. Such oligonucleotides or polynucleotides have tremendous identifiable benefits.

For instance, the claimed oligonucleotides or polynucleotides can be used to expand the utility of current genomic data such as human genomic data. Persons of skill in the art readily recognize the utility, both scientific and commercial, of genomic data from species such as humans and mice. For example, billions of dollars have been invested in the human genome project resulting in useful human genomic data. *See, e.g.*, Venter *et al.*, 2001, Science 291:1304. The results have been a stunning success as the utility of human genomic data has been widely recognized as a great gift to humanity. *See, e.g.*, Jasny and Kennedy, 2001, Science 291:1153. Technology that enhances the utility of useful genomic data is itself useful.

Current genomic data lacks necessary information that would make the data even more useful. For instance, of the myriad putative genes identified by the Human Genome Project, only a relatively small number are known to be expressed. Current technology struggles to separate expressed genes from "junk" DNA in the putative genes identified by massive sequencing efforts.

As disclosed in the specification at pages 1-2, isolated expressed DNA sequences from the human genome have tremendous utility in identifying the expressed genes in raw genomic sequences. Furthermore, the gene trapped sequences of the present invention overcome some of the limitations of conventional cDNA and expressed sequence tag libraries. In particular, the gene trapped sequences of the present invention, including SEQ ID NOS:9-18, were identified using reverse orientation retroviral gene trap vectors that nonspecifically integrate into the target cell genome. These gene trap vectors do not rely solely on the degree of endogenous mRNA expression of a gene for identification of that gene. Hence, the gene trap vectors are able to trap even poorly expressed genes. The identification of gene trapped sequences such as SEQ ID NOS:9-18 thus increases the value and utility of raw genomic data by enabling the identification of expressed genes, even poorly expressed genes, within the genomic data.

Furthermore, the specification provides numerous other credible, specific and substantial utilities for polynucleotides or oligonucleotides comprising SEQ ID NOS:9-18. For example, polynucleotides or oligonucleotides comprising SEQ ID NOS:9-18 can be used for diagnostic gene expression and analysis, for cross species hybridization analysis, antisense inhibition, gene targeting, identifying exon splice junctions, gene therapy, gene delivery and chromosome mapping. Each of these utilities is credible, specific and substantial.

For instance, at page 8, lines 9-16, the specification describes the utility of polynucleotides or oligonucleotides comprising SEQ ID NOS:9-18 for physical and genetic mapping of the human genome and/or the genome of model organisms. To illustrate, early gene mapping techniques relied on methods such as Giemsa staining to identify regions of chromosomes. Giemsa staining, however, suffered from limited resolution. In particular, the human genome could only be divided into as many as 350 to 850 bands by conventional Giemsa staining techniques. The effective resolution of genetic maps based on such techniques was limited to about 5 to 10 megabases.

Hybridization techniques such as fluorescence in situ hybridization revolutionized genetic mapping techniques. With such hybridization techniques the resolution of genetic mapping techniques can be improved to resolutions of about 50 kilobases to 100 kilobases or even greater. However, such mapping techniques based on hybridization require specific

hybridization probes in order to be effective. Polynucleotides or oligonucleotides comprising SEQ ID NOS:9-18 provide additional specific probes that can be used to improve the utility of current genetic mapping techniques. Since the use of a polynucleotide or oligonucleotide comprising one of SEQ ID NOS:9-18 for mapping specifically identifies the genomic location corresponding to the polynucleotide or oligonucleotide, the use is specific for the polynucleotide or oligonucleotide.

Since polynucleotides or oligonucleotides comprising SEQ ID NOS:9-18 can be used to expand the utility of genomic data, to expand the utility of current mapping techniques and for the other utilities discussed above and in the specification, Applicants submit such polynucleotides or oligonucleotides satisfy the requirements for patentability under 35 U.S.C. § 101. Applicants therefore respectfully request that the rejection of Claims 1, 3 and 4 under 35 U.S.C. § 101 be withdrawn. Applicants also submit that new Claims 5 and 6 meet the requirements for patentability under 35 U.S.C. § 101.

V. REJECTION UNDER 35 U.S.C. § 112, FIRST PARAGRAPH (UTILITY)

Claims 1, 3 and 4 stand rejected under 35 U.S.C. § 112, first paragraph, as allegedly lacking utility. Applicants traverse this rejection on the ground that Claims 1, 3 and 4 have significant patentable utility as discussed in Section IV, above. Applicants respectfully request that the rejection of Claims 1, 3 and 4 under 35 U.S.C. § 112, first paragraph, be withdrawn. Applicants also submit that new Claims 5 and 6 meet the requirements for patentability under 35 U.S.C. § 112, first paragraph.

VI. REJECTION UNDER 35 U.S.C. § 112, FIRST PARAGRAPH, (WRITTEN DESCRIPTION)

Claims 1, 3 and 4 stand rejected under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter that was not described in the specification. Applicants traverse this rejection on the ground that amended Claims 1, 3 and 4 are fully supported by the specification and claims as originally filed.

35 U.S.C. § 112, first paragraph, requires that the specification contain a written description of the invention. An applicant must convey with reasonably clarity to those skilled in the art that the applicant was in possession of the invention. *Vas-Cath v. Mahurkar*, 19 USPQ2d 1111, 1117 (Fed. Cir. 1991). An adequate description of a chemical genus

requires a precise definition by *structure, formula, chemical name* or *physical properties* sufficient to distinguish the genus from other materials. *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993). The standard for claims involving chemical materials has been explicitly stated by the Federal Circuit:

> In claims involving chemical materials, generic formulae usually indicate with specificity what the generic claims encompass. One skilled in the art can distinguish such a formula from others and can identify many of the species that the claims encompass. Accordingly, such a formula is normally an adequate description of the claimed genus. *Univ. of California v. Eli Lilly and Co.*, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997).

However, description of the function of genetic material is not an adequate description of the genetic material:

> In claims to genetic material...a generic statement such as "vertebrate insulin cDNA" or "mammalian insulin cDNA," without more, is not an adequate written description of the genus because it does not distinguish the claimed genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. *Id.*

Thus, a claim describing a genus of nucleic acid by *structure, formula, chemical name* or *physical properties* sufficient to distinguish the genus from other materials meets the written description requirement of 35 U.S.C. § 112, first paragraph, as elaborated by the Federal Circuit in *Fiers v. Revel* and in *Univ. of California v. Eli Lilly and Co.*

Claims 1 and 3-6 recite synthetic oligonucleotides or isolated polynucleotides corresponding to one of SEQ ID NOS:9-18. The synthetic oligonucleotides or isolated polynucleotides are fully described by *structure* or by *physical properties*, or both, sufficient to distinguish the claimed synthetic oligonucleotides or isolated polynucleotides from other materials.

For instance, Claim 1 recites synthetic oligonucleotides that comprise a contiguous stretch of at least about 15 nucleotides of at least one of SEQ ID NOS:9-18. Given the description of Claim 1, one of skill in the art can readily distinguish the synthetic oligonucleotides of Claim 1 from other materials by the *structural* description of Claim 1. If a synthetic oligonucleotide comprises a contiguous stretch of at least about 15 nucleotides of at least one of SEQ ID NOS:9-18, the synthetic oligonucleotide is within the genus of

Claim 1. Other chemical materials that lack this *structural* feature are not within the genus. Claims 3-5 similarly recite genera of isolated polynucleotides with precise *structural* definitions of chemical genera.

New Claim 6 recites an isolated polynucleotide capable of hybridizing to a polynucleotide or an oligonucleotide of Claim 1, 2, 4 or 5. New Claim 6 describes a genus of polynucleotides by a *physical property* that readily distinguishes the claimed polynucleotides from other materials. In particular, those polynucleotides with the *physical property* of being capable of hybridizing to a polynucleotide of Claim 1, 2, 4 or 5 are within the genus of Claim 6. Other chemical materials that lack this *physical property* are not within the genus. One of skill in the art can readily distinguish the polynucleotides of Claim 6 from other materials. New Claim 6 thus meets the written description requirement.

Since Claims 1, 3 and 4 meet the written description requirement, Applicants respectfully request that the rejection of Claims 1, 3 and 4 under 35 U.S.C. § 112, first paragraph, be withdrawn. Applicants also submit that new Claims 5 and 6 meet the requirements for patentability under 35 U.S.C. § 112.

VII. THE REJECTIONS UNDER 35 U.S.C. § 102

Claims 1 stands rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Adams et al., 1997, Accession No. AC002043 ("Adams") or by Hillier et al., 1996, Accession No. H69406 ("Hillier"). Claim 2 stands rejected under 35 U.S.C. § 102(a) and under 35 U.S.C. § 102(b) as allegedly being anticipated by several references. Since Claim 2 has been canceled without prejudice, Applicants submit that the rejections of Claim 2 are moot.

The standard for anticipation under 35 U.S.C. §102 is strict identity. Anticipation under § 102 can only be established by a single prior art reference that teaches each and every element of the claimed invention. *Structural Rubber Products Co. v. Park Rubber Co.* 223 USPQ 1264 (1984).

Adams does not teach or suggest each and every element of amended Claim 1. Amended Claim 1 recites a synthetic oligonucleotide comprising a contiguous stretch of at least about 15 nucleotides of at least one of SEQ ID NOS:9-13, 15, 17, 18. Adams does not teach or suggest a synthetic oligonucleotide comprising a contiguous stretch of at least about 15 nucleotides of at least one of SEQ ID NOS:9-13, 15, 17, 18. The PTO asserts that Adams discloses a nucleic acid sequence that comprises at least about 15 contiguous nucleotides of

SEQ ID NO:13. However, the PTO provides no evidence to support this assertion, and, in fact, Adams has no significant homology to SEQ ID NO:13.

Hillier also does not teach or suggest each and every element of amended Claim 1. Amended Claim 1 recites a synthetic oligonucleotide comprising a contiguous stretch of at least about 15 nucleotides of at least one of SEQ ID NOS:9-13, 15, 17, 18. Hillier does not teach or suggest a synthetic oligonucleotide comprising a contiguous stretch of at least about 15 nucleotides of at least one of SEQ ID NOS:9-13, 15, 17, 18.

Since Adams and Hillier do not teach or suggest each and every element of amended Claim 1, Adams and Hillier do not anticipate Claim 1. Applicants request that the rejections of Claim 1 under 35 U.S.C. § 102(b) be withdrawn.

CONCLUSION

Applicants submit that Claims 1 and 3-6 satisfy all of the criteria for patentability and are in condition for allowance. An early indication of the same and passage of Claims 1 and 3-6 to issuance is therefore kindly solicited.

No fees in addition to the extension fee are believed due in connection with this response. However, the Commissioner is authorized to charge all required fees, fees under 37 C.F.R. § 1.17 and all required extension of time fees, or credit any overpayment, to Pennie & Edmonds U.S. Deposit Account No. 16-1150.

Respectfully submitted,

Date: April 11, 2001

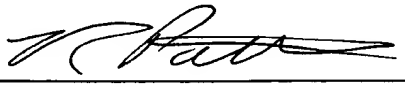

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Exhibit A
Marked Up Version of Amended Claims

1. (Amended) A synthetic oligonucleotide comprising a contiguous stretch of at least about 15 nucleotides [first disclosed in] of at least one of SEQ ID NOS:[9-1008]9-13, 15, 17, 18.

3. (Amended) An isolated polynucleotide comprising a contiguous stretch of at least about 60 nucleotides [first disclosed in] of at least one of SEQ ID NOS:[9-1008]9-18.

4. (Amended) An isolated polynucleotide according to Claim 3, wherein said polynucleotide sequence comprises at least one of SEQ ID NOS:[9-1008]9-18.

Exhibit B
Pending Claims

1. (Amended) A synthetic oligonucleotide comprising a contiguous stretch of at least about 15 nucleotides of at least one of SEQ ID NOS:9-13, 15, 17, 18.

3. (Amended) An isolated polynucleotide comprising a contiguous stretch of at least about 60 nucleotides of at least one of SEQ ID NOS:9-18.

4. (Amended) An isolated polynucleotide according to Claim 3, wherein said polynucleotide sequence comprises at least one of SEQ ID NOS:9-18.

5. (New) A synthetic oligonucleotide comprising a contiguous stretch of at least about 20 nucleotides of SEQ ID NO:16.

6. (New) An isolated polynucleotide capable of hybridizing to a polynucleotide or an oligonucleotide of Claim 1, 3, 4 or 5 under high stringency conditions.